REMARKS

Claims 28-29, 32-35 and 47-49 remain in the application. Claims 28, 29, 33-35 and 47 have been amended. Reexamination and allowance of the amended claims are requested.

The Examiner has rejected claims 28-29, 32-35 and 47-49 under 35 U.S.C. § 112, second paragraph, as indefinite. In response, claim 28 has been amended to eliminate the recitation of "having", and claim 47 has been amended to recite "comprising." Claims 34 and 35 have been amended to recite "nucleic acid" to reflect the proper antecedent.

The Examiner has rejected claims 33-35 and 48-49 under 35 U.S.C. § 112, first paragraph, for lack of disclosure in the specification as filed. The Examiner asserts that the recitation of "a fusion of at least two of an oligonucleotide, a polynucleotide, and a gene having a nucleotide sequence of at least part of a T-gene" constitutes new matter. However, the expression "T-gene" is used to indicate all members of the novel *PLAG* gene family of the invention and their corresponding translocation or fusion partner, such as *CTNNB1* (see page 5, lines 10-13 of the present specification). Therefore, both *PLAG* and *CTNNB1* are T-genes according to the invention. In addition, Example 2 of the present specification describes how to make and/or isolate *PLAG1/CTNNB1* and *CTNNB1/PLAG1* fusion transcripts from tumors, which are further illustrated in Figure 6. Therefore, references to "a fusion...of at least part of a T-gene" do not constitute new matter. For these reasons, it is believed that the rejection of claims 33-35 and 48-49 for lack of disclosure has been overcome.

The Examiner has rejected claims 28-29, 32-35 and 47-49 under 35 U.S.C. § 112, first paragraph, for inadequate written description. The Examiner has also rejected these claims under 35 U.S.C. § 112, first paragraph for lack of enablement. The Examiner asserts that, while the specification is enabling for the cDNA sequence of the *PLAG1* gene, no reasonable enablement is provided for the following:

(1) a nucleic acid in isolated form, wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene having a sequence of at least part of the *PLAG1* gene, a sequence complementary thereto or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide sequence of *PLAG1* in the region from zinc fingers 4 to 7 (e.g., claims 47 and claims depending thereon),

(2) a nucleic acid having homology with the zinc finger domains, the *PLAG1* gene or the complementary strand thereof, including modified, degenerate, or elongated versions of both strands (e.g., claim 28), and

(3) a macromolecule comprising at least one of the *CTNNB1* gene and fusions thereof (e.g., claims 33 and 47 and claims depending thereon).

The Examiner concludes that the specification fails to provide information to enable one of ordinary skill in the art to make or use the claimed nucleic acid and using the large number of undisclosed nucleotide variations encompassed by the claims. Further, according to the Examiner, the claimed invention provides insufficient guidance and directions for one skilled in the art to make and use the claimed invention without undue experimentation. Further, the Examiner alleges that the claimed invention lacks proper working examples and is of the opinion that the skilled practitioner is not able to reproduce the results as reported in the specification.

Accordingly, Applicants provide the following analysis of each of the variants of nucleic acids as presented in the claims.

"a sequence complementary thereto"

Claim 47 has previously been amended to specify that a protein encoded by the claimed nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide sequence of *PLAG1* in the region from zinc fingers 4 to 7. Because a complementary sequence is derived in an unambiguous fashion on a nucleotide-by-nucleotide basis from a given sequence, no ambiguity is introduced by claims drawn to a complementary sequence. Although the sequences provided according to the present invention are only represented by one strand (from 5' to 3'), it is clear to one skilled in the art what is meant by and how to define the sequence of "the complementary sequence."

"an antisense version thereof"

A basis for antisense versions is provided in Example 12 of the specification, wherein it is shown that inhibition of *PLAG1* expression in tumor cells can be obtained by using antisense *PLAG1* constructs.

"a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide sequence of *PLAG1* in the region from zinc fingers 4 to 7"

Certain proteins of the present invention are characterized by the presence of a specific zinc finger sequence, and no sequence similarity was found to any known zinc finger protein in the prior art (see page 41, lines 10-11 of the present specification). In addition, in Example 2, point 3.2, methods are disclosed for finding sequences with unknown functions and assembling these sequences into aligned nucleic acids with sequence similarities of about 75% at the amino acid level.

"nucleic acid having homology with the zinc finger domains of the *PLAG1* gene"

Claim 28 has been amended so that the "homology" recited therein is analogous to the "homology" of claim 47, being at least 75% in the region from zinc fingers 4 to 7 at the amino acid level.

"modified versions of both strands"

This terminology has been removed from claims 28 and 29.

"degenerate versions of both strands"

This terminology has been removed form claims 28 and 29. Applicants note that the existence of degenerate sequences and their ability to produce identical proteins are well established. Therefore, it is understood that specific nucleic acid sequences embrace degenerate sequences.

"elongated versions of both strands"

References to elongated versions of both strands have been deleted from claim 28 and 29.

"macromolecule comprising at least part of the *CTNNB1* gene and fusions thereof"

References to fusions of a macromolecule comprising at least part of the *CTNNB1* gene have been deleted from claim 33.

Applicants have thus referred to the basis in the specification for, have provided explanation for, or have cancelled claim language objected to by the Examiner. Accordingly,

the rejection of claims 33-35 and 48-49 for lack of disclosure, and the rejection of claims 28-29, 32-35 and 47-49 for inadequate written description are believed to have been overcome.

The Examiner has rejected claim 33 under 35 U.S.C. § 102(b) for anticipation by Kraus et al. (*Genomics* **23**: 272-274, 1994) (hereinafter "Kraus"). The Examiner asserts that claim 33 is drawn to a macromolecule comprising a nucleic acid isolated form, comprising one of an oligonucleotide, a polynucleotide and a gene having a nucleotide sequence of at least part of a T-gene selected from the group consisting of the *PLAG1* subfamily of zinc finger protein genes, and at least part of the *CTNNB1* gene and fusions thereof, or complementary degenerate versions of the nucleotide sequence, and that Kraus discloses this embodiment. However, Kraus makes reference only to species containing portions of the *CTNNB1* gene, not to fusions containing portions of the *PLAG1* subfamily of zinc finger protein genes. Claim 33 has been amended to emphasize that the claimed species are fusions that must contain a nucleic acid that is part of a *PLAG1* gene and a nucleic acid that is part of the *CTNNB1* gene. Kraus does not teach or suggest fusions incorporating nucleic aids of both a *PLAG1* gene and the *CTNNB1* gene. For these reasons, it is believed that the rejection of claims 33 for anticipation by Kraus has been overcome.

The Examiner has rejected claims 33–35 under 35 U.S.C. § 102(a) for anticipation by Nollet et al. (*Genomics* **32**: 413-424, 1996) (hereinafter "Nollet"). The Examiner asserts that claim 33, drawn to a macromolecule comprising a nucleic acid isolated form, comprising one of an oligonucleotide, a polyncleotide and a gene having a nucleotide sequence of at least part of a T-gene selected from the group consisting of the *PLAG1* subfamily of zinc finger protein genes, and at least part of the *CTNNB1* gene and fusions thereof, or complementary degenerate versions of the nucleotide sequence, represents an embodiment disclosed by Nollet. The Examiner also asserts that Nollet anticipates the derivative of claim 34 and the labeled derivative of claim 35. However, Nollet refers only to the *CTNNB1* gene, and not to the *PLAG1* subfamily of zinc finger

protein genes. Claim 33 has been amended to emphasize that the claimed species are fusions that must contain a nucleic acid that is part of a *PLAG1* gene and a nucleic acid that is part of the *CTNNB1* gene. Nollet does not teach or suggest fusions incorporating nucleic aids of both a *PLAG1* gene and the *CTNNB1* gene. For these reasons, it is believed that the rejection of claims 33–35 for anticipation by Nollet has been overcome.

In view of the above amendments and remarks, it is believed that the claims are in condition for allowance. Reconsideration of the rejections is requested. Allowance of claims 28, 29, 32-35 and 47-49 is respectfully requested.

Respectfully submitted,

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MARKED-UP VERSION OF THE CLAIMS

28. (Twice Amended) The nucleic acid as claimed in claim 47, [having homology] wherein the nucleic acid is homologous with the zinc finger domains of the *PLAG1* (pleomorphic adenoma gene 1) gene the nucleotide sequence of which is depicted in figure 4A (SEQ ID NO: 116), or a complementary strand thereof, [including modified, degenerate or elongated versions of both strands] and wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide sequence of *PLAG1* in the region from zinc fingers 4 to 7.

29. (Thrice Amended) The nucleic acid as claimed in claim 47, comprising the nucleotide sequence of the *PLAG1* gene as depicted in figure 4A (SEQ ID NO: 116), or a complementary strand thereof[, including modified, degenerate or elongated versions of both strands].

33. (Thrice Amended) A macromolecule comprising a nucleic acid in isolated form, comprising a fusion of at least two of an oligonucleotide, a polynucleotide and a gene [having], wherein at least a first one comprises a nucleotide sequence of at least part of a T-gene selected from the group consisting of the *PLAG* (pleomorphic adenoma gene 1) subfamily of zinc finger protein genes, and wherein at least a second one comprises at least part of the *CTNNB1* (β catenin) gene [and fusions thereof], or complementary or antisense versions of the nucleotide sequence.

34. (Once Amended) The macromolecule as claimed in claim 33, wherein the [derivative] nucleic acid is selected from the group consisting of:

a) a transcript corresponding to the nucleic acid;

b) cDNA corresponding to the nucleic acid;

c) sense or antisense DNA corresponding to the nucleic acid;

d) a nucleic acid including a gene, or a derivative thereof, isolated by using at least part of a T-gene as one of a probe or primer;

e) a protein encoded by the nucleic acid; and

f) antibodies, or derivatives thereof, directed to the nucleic acid, the transcript, the cDNA and the protein.

35. (Once Amended) The macromolecule as claimed in claim 34, wherein the [derivative] nucleic acid is labeled.

47. (Thrice Amended) A nucleic acid in isolated form, wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene [having] comprising a sequence of at least part of the *PLAG1* (pleomorphic adenoma gene 1) gene, or the complementary sequence or antisense version of the nucleic acid; wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide sequence of [PLAG 1] *PLAG1* in the region from zinc fingers 4 to 7.